SDL

PATENT COOPERATION TREA

DOCKETED ES

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

To:

SANDERS, Deirdre, E.
Hamilton, Brook, Smith & Reynolds, P.C.
530 Virginia Road
P.O. Box 9133
Concord, MA 01742-9133
ETATS-UNIS D'AMERIQUE

Date of mailing *(day/month/year)* 09 February 2006 (09.02.2006)	
Applicant's or agent's file reference 3518.1015002	IMPORTANT NOTICE

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/024725	30 July 2004 (30.07.2004)	30 July 2003 (30.07.2003)

Applicant
DEPUY SPINE, INC. et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

Rec'd IFD
RECEIVED
FEB 16 2006
HAMILTON, BROOK
SMITH & REYNOLDS, P.C.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Simin Baharlou
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 71 30

Form PCT/IB/326 (January 2004)

C161

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 3518.1015002	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2004/024725	International filing date *(day/month/year)* 30 July 2004 (30.07.2004)	Priority date *(day/month/year)* 30 July 2003 (30.07.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant DEPUY SPINE, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 15 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 30 January 2006 (30.01.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Simin Baharlou Telephone No. +41 22 338 71 30

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/US2004/024725	International filing date *(day/month/year)* 30.07.2004
Priority date *(day/month/year)* 30.07.2003	
International Patent Classification (IPC) or both national classification and IPC A61K31/436, A61K38/30, A61K31/198, A61K39/395, A61P19/02	
Applicant DEPUY SPINE, INC.	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	A. Jakobs Telephone No. +31 70 340-2617

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/024725

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☐ The following document has not been furnished:

   ☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ The International Searching Authority has not been able to consider the validity of the priority claim because a copy of the earlier application whose priority has been claimed was not available to the International Searching Authority at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-11,30,34-75,80-82 (partially) 12-29,31-33,76-79,83

because:

☒ the said international application, or the said claims Nos. 1-11,30,34-75,80-82 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-11,30,34-75,80-82 (partially) 12-29,31-33,76-79,83

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-4,30,34-66,80-82 (partially) 5-11,67-75

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	-
	No:	Claims	1-11,30,34-75,80-82
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-11,30,34-75,80-82
Industrial applicability (IA)	Yes:	Claims	see separate sheet
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III.

Claims 1-11,30,34-75,80-82 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Present claim 1-11,30,34-75,80-82 relate to a method defined by reference to the following parameters:
an inhibitor of a pro-inflammatory interleukin, an inhibitor of a pro-inflammatory interleukin wherein the interleukin is IL-1, IL-1beta, IL-2, IL-6, IL-8, IL-12, IL-19.
The use of these parameters in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to compare the parameters the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search has been restricted to the use of the inhibitors specifically mentioned in the description on page 19, lines 20-24, i.e. Kineret, IL1-Receptor Type 2 and IL-1 Trap.

No Written Opinion will be formulated with respect to subject matter which is not covered by the search report.

Re Item IV.

The separate inventions/groups of inventions are:

1. Claims 1-4,30,34-66,80-82 (partially) 5-11,67-75
   Use of an inhibitor of a pro-inflammatory interleukin for the manufacture of a medicament for treating an inflamed orthopedic joint.

2. Claims 1-4,30,34-66,80-82 (partially) 12-15,76-79,83
   Use of an inhibitor of TNF-alpha synthesis, an inhibitor of membrane-bound TNF-alpha or an inhibitor of a natural receptor of TNF-alpha for the manufacture of a medicament for treating an inflamed orthopedic joint.

3. Claims 1-4,30,34-65,80-82 (partially) 19-21
Use of an inhibitor of NO synthase for the manufacture of a medicament for treating an inflamed orthopedic joint.

4. Claims 1-4,30,34-65,80-82 (partially) 22
Use of an inhibitor of PLA2 enzyme for the manufacture of a medicament for treating an inflamed orthopedic joint.

5. Claims 1-4,30,34-65,80-82 (partially) 23-27
Use of an inhibitor of an anti-proliferative agent for the manufacture of a medicament for treating an inflamed orthopedic joint.

6. Claims 1-4,30,34-65,80-82 (partially) 28
Use of an anti-oxidant for the manufacture of a medicament for treating an inflamed orthopedic joint.

7. Claims 1-4,30,34-65,80-82 (partially) 31-33
Use of an apoptosis inhibitor for the manufacture of a medicament for treating an inflamed orthopedic joint.

8. Claims 1-4,30,34-65,80-82 (partially) 29
Use of an inhibitor of MMP for the manufacture of a medicament for treating an inflamed orthopedic joint.

9. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a diaryl imidazole for the manufacture of a medicament for treating an inflamed orthopedic joint.

10. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a diaryl N,N' diaryl urea or a N,N-diarylurea for the manufacture of a medicament for treating an inflamed orthopedic joint.

11. Claims 1-4,16,17,30,34-65,80-82 (partially)

Use of an inhibitor of p38 kinase wherein the compound is a benzophenone for the manufacture of a medicament for treating an inflamed orthopedic joint.

12. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a pyrazole ketone for the manufacture of a medicament for treating an inflamed orthopedic joint.

13. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a indole amide for the manufacture of a medicament for treating an inflamed orthopedic joint.

14. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a diamide for the manufacture of a medicament for treating an inflamed orthopedic joint.

15. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a quinazoline for the manufacture of a medicament for treating an inflamed orthopedic joint.

16. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a pyrimido[4,5-d]pyrimidinone for the manufacture of a medicament for treating an inflamed orthopedic joint.

17. Claims 1-4,16,17,30,34-65,80-82 (partially)
Use of an inhibitor of p38 kinase wherein the compound is a pyridylamino-quinazoline for the manufacture of a medicament for treating an inflamed orthopedic joint.

18. Claims 1-4,30,34-65,80-82 (partially) 18
Use of an inhibitor of a 1-aryl-2-pyridinyl heterocycle as specified in claim 18 for the manufacture of a medicament for treating an inflamed orthopedic joint.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The problem to be solved by the present application is to provide for the treatment of inflamed orthopedic joints.

The proposed solution is to use a compound selected from
i) an inhibitor of a pro-inflammatory interleukin;
ii) an inhibitor of TNF-alpha synthesis;
iii) an inhibitor of membrane-bound TNF-alpha,
iv) an inhibitor of a natural receptor of TNF-alpha,
v) an inhibitor of NO synthase;
vi) an inhibitor of PLA2 enzyme;
vii) an anti-proliferative agent;
viii) an anti-oxidant,
ix) an apoptosis inhibitor selected from the group consisting of EPO mimetic peptides, EPO mimetibodies, IGF-I , IGF-II, and caspase inhibitors,
x) an inhibitor of MMPs,
xi) an inhibitor of p38 kinase, said inhibitor being a
a) diaryl imidizole (sic)
b) N,N'-diaryl urea;
c) N,N-diaryl urea;
d) benzophenone;
e) pyrazole ketone;
f) indole amide;
g) diamides;
h) quinazoline;
1) pyrimido[4,5-d]pyrimidinone
j) pyridylamino-quinazoline.
or
xii) a 1-aryl-2-pyridinyl heterocycle selected from the group consisting of:
a) 4,5 substituted imidazole;
b) 1,4,5 substituted imidizole;
c) 2,4,5 substituted imidizole;
d) 1,2,4,5 substituted imidizole; and
e) non-imidizole 5-membered ring heterocycle.

Said compounds may be administered trans-capsularly, closely adjacent to the outer wall of the capsule or at a location closely adjacent to an outer wall of the capsule. See claims 1, 47, 60.

US5368841 discloses local i.e. intracapsular injection of drugs for treating inflammatory joint conditions. See the passages cited in the search report.

US2001016195 discloses antagonists of IL-1, IL-6, IL-8 to treat osteoarthritis and other forms of arthritis including rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis. Said treatment comprises localized administration, including perilesional or intralesional administration of compounds including interleukin 1 receptor antagonist (IL-1 RA) (Amgen) and interleukin 1 receptor type II (IL-1R type II) (Immunex). See the passages cited in the search report.

WO0185179 discloses dextran based composition for injecting into damaged or diseased joints, filling cavities and spaces in artificial joints, applying to joints in connection with post-surgical procedures and injected into joint injury. See the passages cited in the search report.

EP438234 discloses the intrasynovial administration of antithrombin in relation to the treatment of arthritis. See the passages cited in the search report.

US4427649 discloses compsns. useful for treating rheumatoid inflammations of the synovial joints, since they can be injected directly into the cavity of the joint. See the passages cited in the search report.

US6294170 discloses the intracapsular administration of an inhibitor of IL-1, preferably IL-1ra, either alone or in combnation with another drug for treating inflammatory joint diseases. See the passages cited in the search report.

Furthermore, the compounds of the proposed solutions do not share a significant structural element, nor do they belong to a same recognized class of chemical compounds.

According to Article 3(4)(iii) PCT, an international application shall comply with "the

prescribed requirement of unity of invention". This means, as explained in Rule 13.1 PCT, that the application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

From the above cited documents, it appears that the use of above specified compounds in relation to the treatment of above specified disorders is known in the prior art and can not fulfil the role of special technical feature (general inventive concept) in the sense of Rule 13.2 PCT.

Accordingly there is no new technical effect linking the different groups of inventions.

In the present application no further technical feature can be distinguished that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions.

Consequently the present application lacks unity of invention.

As searching the other inventions would have caused a major additional searching effort, only the first invention was searched.

As the applicant has not had a search report drawn up on the other inventions, this opinion relates only to the invention in respect of which a search report has been carried out, in other words the invention first mentioned in the claims.

Re Item V.

1 The following documents are referred to in this communication:

D1: WO 97/28828 A (AMGEN BOULDER INC; COLLINS, DAVID, S; BEVILACQUA, MICHAEL, P) 14 August 1997 (1997-08-14)

D2: WO 98/24477 A (AMGEN INC; BENDELE, ALISON, M; SENNELLO, REGINA, M) 11 June 1998 (1998-06-11)

D3: US-B1-6 294 170 (BOONE THOMAS C ET AL) 25 September 2001 (2001-09-25)

D4: EP-A-1 133 995 (THE UNIVERSITY OF COLORADO FOUNDATION, INC; AMGEN INC; SYNERGEN, INC) 19 September 2001 (2001-09-19)
D5: GABAY C: "IL-1 TRAP" CURRENT OPINION IN INVESTIGATIONAL DRUGS, CURRENT DRUGS, LONDON, GB, vol. 4, no. 5, May 2003 (2003-05), pages 593-597, XP009017868 ISSN: 0967-8298
D6: DAYER J-M: "THE PIVOTAL ROLE OF INTERLEUKIN-1 IN THE CLINICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS" RHEUMATOLOGY, OXFORD UNIVERSITY PRESS, LONDON, GB, vol. 42, no. SUPPL 2, May 2003 (2003-05), pages II03-II10, XP008041555 ISSN: 1462-0324
D7: US 2001/016195 A1 (TOBINICK EDWARD L) 23 August 2001 (2001-08-23)
D8: US-A-5 368 841 (TRAUNER ET AL) 29 November 1994 (1994-11-29)
D9: WO 01/85179 A (CLEMSON UNIVERSITY) 15 November 2001 (2001-11-15)
D10: EP-A-0 438 234 (KITA, KIYOSHI) 24 July 1991 (1991-07-24)
D11: US-A-4 427 649 (DINGLE ET AL) 24 January 1984 (1984-01-24)

2 CLAIMS 1-11,30,34-75,80-82

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-11,30,34-75,80-82 is not new in the sense of Article 33(2) PCT.
Document D1 discloses (see the passages cited in the search report) the intracapsular administration of an inhibitor of IL-1, preferably IL-1ra, either alone or in combination with another drug for treating inflammatory joint diseases.

2.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-11,30,34-75,80-82 is not new in the sense of Article 33(2) PCT.
Document D2 discloses (see the passages cited in the search report) the intracapsular administration of an inhibitor of IL-1, preferably IL-1ra, either alone or in combination with another drug for treating inflammatory joint diseases.

2.3 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-11,30,34-75,80-82 is not new in the sense of Article 33(2) PCT.

Document D3 discloses (see the passages cited in the search report) the intracapsular administration of an inhibitor of IL-1, preferably IL-1ra, either alone or in combination with another drug for treating inflammatory joint diseases.

2.4 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-11,30,34-75,80-82 is not new in the sense of Article 33(2) PCT.
Document D4 discloses (see the passages cited in the search report) the use of Kineret (anakinra; N(sup 2)-L-methionyl- Interleukin 1 receptor antagonist (human isoform x reduced)) in relation to the treatment of inflammatory joint diseases.

2.5 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-11,30,34-75,80-82 is not new in the sense of Article 33(2) PCT.
Document D5 discloses (see the passages cited in the search report) the use of IL-trap in relation to the treatment of rheumatoid arthritis.

2.6 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-11,30,34-75,80-82 is not new in the sense of Article 33(2) PCT.
Document D6 discloses (see the passages cited in the search report) that Kineret (IL-1ra) offers a new therapeutic modality for rheumatoid arthritis, IL-1 can also be antagonized by the decoy receptor IL-1RII.

2.7 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-11,30,34-75,80-82 is not new in the sense of Article 33(2) PCT.
Document D7 discloses (see the passages cited in the search report) that antagonists of IL-1, IL-6, IL-8 are used to treat osteoarthritis and other forms of arthritis including rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis. Said treatment comprises localized administration, including perilesional or intralesional administration of compounds including interleukin 1 receptor antagonist (IL-1 RA) (Amgen) and interleukin 1 receptor type II (IL-1R type II) (Immunex).

2.8 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.
Document D8-D11 disclose (see the passages cited in the search report) local i.e. intracapsular injection of drugs for treating inflammatory joint conditions.

3 CLAIMS 1-11,30,34-75,80-82

Claims 1-11,30,34-75,80-82 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT). D1-D3, D7-D11 disclose methods of treating an inflamed orthopedic joint comprising the intracapsular adminstration of drugs, i.e. inhibitors of proinflammatory interleukins. Therefore said claims, as far as novel, can not be considered to involve an inventive step.